REMARKS

Claims 1-3 and 10-13 are now in the application, of which claim 1 is generic.

The objection to the specification and rejection of the claims under the first paragraph of 35 U.S.C. 112 have been obviated by the amendment to specification deleting reference to "tumors and psoriasis" and the cancellation of the method claims and pharmaceutical composition claims as apparently suggested by the Examiner.

Also, as suggested by the Examiner, the specification has been amended to include the status of parent application S.N. 202,512.

The rejection of claim 9 under 35 U.S.C. 203 is no longer applicable since claim 9 has been cancelled and no claim has been presented which recites the process of preparing the claimed compounds.

Claims 1-8 were rejected under 35 U.S.C. 103 over British patent 1345502 to Elslager, et al. Elslager, et al. fail to suggest or render obvious the present invention. In particular, among other things, Elslager, et al. fail to teach the specific salts required by the present invention and fail to suggest the combination of properties possessed by the specific salts of the present invention.

Elslager, et al. suggest the free base of the two compounds of the present invention and on page 2, column 2, state that salts may be formed from various organic acids.

However, salts of 2-hydroxyethane-sulfonic acid (i.e. - isethionic) and glucuronic acid as required by the present invention are not even mentioned in the list of acids suggested by Elslager, et al.

Furthermore, the properties possessed by the specific

salts of the present invention are not even remotely suggested by Elslager, et al. In addition, Berge, et al. fail to overcome the deficiency of Elslager, et al. since Berge, et al. do not provide sufficient incentive or direction to persons skilled in the art to employ the isethionic acid or glucuronic acid to obtain the salts possessing the combination of properties achieved by the present invention.

According to the present invention, in order to obtain salts of 2,4,diamino-5-methyl-6-[(3,4,5-trimethoxyanilino)-methyl]-quinazoline which have a satisfactory degree of solubility in water, are stable, non-toxic, and are pharmaceutically acceptable, it is necessary to use isethionic acid or glucuronic acid. Of the large number of salts made and examined, only two satisfied applicant's standards for being pharmaceutically acceptable and highly water soluble (see Tables I-III in view of paragraph 3 on page 4). The various acid addition salts as shown in the Tables, other than the two claimed herein, proved to be unsatisfactory. In fact, a number of acid salts suggested in Elslager, et al. including the salts of hydrochloric acid, sulfuric acid, acetic acid, citric acid, tartaric acid, lactic acid, and gluconic acid were tested and found unsuitable.

In addition, the Examiner's attention is directed to page 4, paragraph 3 of the specification which further discusses the undesirability of various salts other than those of the present invention and the reasons therefore.

In point of fact, before the two acid addition salts of this invention were made, one could not be certain that any satisfactory acid addition salts exist. Nothing in the record suggests that one would look to the monoisethionate or glucuronate salt as the solution to the problem.

Since a compound and its properties are inseparable, no property can be ignored in determining patentability and comparing the claimed invention to the prior art. Along these lines,

see In re Papesch 137 U.S.P.Q. 43 (CCPA 1963); In re Burt, et al. 148 U.S.P.Q. 548 (CCPA 1966); In re Ward 141 U.S.P.Q. 227 (CCPA 1964); and In re Cescon 177 U.S.P.Q. 264 (CCPA 1973). Moreover, the properties of the subject matter and improvements which are inherent in the claimed subject matter and disclosed in the specification are to be considered when evaluating the question of obviousness under 35 U.S.C. 103. See In re Antonie 195 U.S.P.Q. 6 (CCPA 1077), In re Estes 164 U.S.P.Q. 519 (CCPA 1070, and In re Papesch, supra.

The prior art fails to provide the necessary incentives or direction to suggest to a person skilled therein to provide the 2-hydroxyethanesulfonic acid addition salt or glucuronic acid addition salt of 2,4-diamino-5-methyl-6-[(3,4,5-trimethoxyanilino)-methyl]-quinazoline to obtain soluble salts possessing the improved characteristics discussed hereinabove. See In re Mercier CCPA ; 515 F.2d 1161, 185 U.S.P.Q. 774 (CCPA 1975); In re Naylor 54 CCPA 902, 369 F.2d 765, 152 U.S.P.Q. 106 (CCPA 1966); and In re Pye, et al. 53 CCPA 877, 355 F.2d 641, 148 U.S.P.Q. 426 (CCPA 1966). The prior art lacks the necessary degree of predictability of success of providing the improved salts needed to sustain a rejection under §103. See In re Mercier, supra, and In re Naylor, supra. The cited references do not suggest, for instance, that combination of high solubility, stability, and non-toxicity.

In light of the above stated reasons and the amending of the specification and claims, it is believed that the application in its present form, is in condition for allowance. A favorable action is respectfully solicited.

Respectfully submitted,

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